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Benzedrine is a compound of the epinephrine series resembling ephedrine and has the chemical formula $C_6H_5CH_2CHNH_2CH_3$. Recently this drug has been manufactured commercially as benzedrine sulphate and offered for sale through the channels of the ordinary drug store. As a result a rather large number of people, including many college students, have resorted to its use in order to keep awake for short and sometimes for rather extended periods of time while preparing for examinations, etc. However, knowledge of the exact nature of the physical and mental effects of this drug on the human organism is at the present time extremely limited.

The therapeutic value of benzedrine in the treatment of narcolepsy has been reported by Prinzmetal and Bloomberg (1). By use of dosages varying from 10 mg. once a day to 40 mg. three times a day the authors report complete relief for nine patients. The benzedrine was found to be approximately three times as effective as ephedrine, and, unlike ephedrine, to have no diminution in effectiveness with long usage. Ulrich, Trapp and Vidgoff (2) using a daily dosage of from 20 to 50 mg. of benzedrine orally report success in the treatment of six cases of narcolepsy. Myerson and Ritvo (3) have found benzedrine sulphate of great value in diminishing or abolishing spasm of the gastro-intestinal tract in roentgen investigations of the stomach and intestine. In the treatment of 200 patients using a dosage of from 10 to 40 mg. they report a severe reaction in only one instance and unpleasant effects in a very small number of cases. The effect is reported to begin in about ten minutes, reaching its height in 15 to 30 minutes and lessening within an hour. A moderate rise in blood pressure was found to occur in most cases and caution is recommended in cases of severe cardiac disease.

Nathanson (4) has studied the effects of benzedrine with 40 patients who complained of exhaustion and who tired easily. Most of the patients did not suffer from organic disease but were diagnosed

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as nervous exhaustion. The majority of the patients received 20 mg. of benzedrine and in approximately 80 per cent of the cases a marked improvement from fatigue was found. In regard to mental effects of the drug the author makes the following statement: "A sense of increased energy and capacity for work was noted in more than half of the cases. In addition a feeling of exhilaration and sense of well being was a consistent effect. This followed repeatedly after the ingestion of the drug. In a few patients there was a secondary depression following the initial stimulation. Many patients volunteered that there had been a definite increase in mental activity and efficiency. Another striking reaction was a tendency to loquaciousness. This was very marked in many instances and was noted both by the patients and by those about them." The drug was also given to a group of 55 normal subjects and to a control group of 25 normal subjects were given tablets of the same appearance containing lactose. By means of a questionnaire the most frequent effect was found to be a sense of well being and a feeling of exhilaration which occurred in more than two-thirds of the subjects. Next in order of frequency was a lessened fatigue, talkativeness, and increased energy and capacity for work. Regarding the regular use of this drug the author issues the following caution. "A definite possibility of a harmful effect exists in that prolonged administration may result in an increased activity and energy expenditure beyond the capacity of some individuals. This is particularly likely since the protective and retarding influence of fatigue is lost."

The present study represents a preliminary attempt to determine the effects of benzedrine sulphate upon mental operations, using written multiplication problems to measure the subject's efficiency. The problems consisted of 64 examples, with three digits in the multiplicand and three digits in the multiplier, mimeographed on four sheets of 8½" by 11" paper with 16 problems evenly spaced on a sheet. The numbers making up the problems were selected in random order, except that no zeros were employed and the number "1" appeared only in the multiplicand. The subjects were six undergraduates and four graduate students at the University of Minnesota. Three of the graduate students were men, 23, 24, and 25 years of age, while the fourth graduate student was a woman 22 years of age. The six undergraduates were all men ranging from 20 to 23 years of age.

The testing was carried on by the authors between April 14 and May 30, 1936. There was no definite interval between the successive trials; however, most of the testing occurred on alternate days. The

amount of benzedrine administered each day was 20 mg. for all subjects, and 20 mg. of lactose was used in the control pills.² Only one trial was given per day and during the periods when the benzedrine and lactose pills were administered there was always a one-day interval between the successive trials and never more than a three-day interval. All of the undergraduate subjects were tested in the afternoon between the hours of 1:30 and 3:00 o'clock and the graduate subjects were tested between 3:00 and 6:00 o'clock. All of the subjects took both the benzedrine and lactose pills between twenty and thirty minutes before lunch. No control was exercised over the diet of the subjects, but all of them ate lunch between 11:45 a. m. and 1:15 p. m., the majority having lunch at about 12:30 p. m.

The procedure employed was to present the four sheets of material to the subject with instructions to work rapidly and accurately as many problems as possible in the twelve minute working period. The four sheets were presented in random order so that the subject did not do the problems in the same sequence on successive trials. Each subject was tested in the same room on every occasion, the place of testing being a quiet, well-lighted room free from distraction.

The ten subjects were divided into three groups, two groups of undergraduate students and one group of graduate students. Group I, the first group of undergraduates, consisted of three subjects who were given five trials at the beginning of the experiment without pills, three trials with benzedrine sulphate pills, three trials with lactose pills and finally three trials without pills. Group II consisted of the other three undergraduates who were given four trials without pills, three trials with benzedrine sulphate pills, three trials with lactose pills, and then three without pills. Group III consisted of four graduate subjects who were given six trials without pills, three trials with benzedrine pills, three trials with lactose pills and three trials without pills.

Below are presented the data showing the average number of problems completed in twelve minutes under various conditions as indicated.

GROUP I

No. Pills	Trials 1 to 5	33.7, 33.0, 36.3, 38.0, 40.0
Benzedrine Sulphate	Trials 6 to 8	41.0, 41.3, 46.3
Lactose Control Pills	Trials 9 to 11	42.7, 42.7, 42.0
No. Pills	Trials 12 to 14	44.0, 43.3, 43.7

² Although the subjects were not told on which trials the benzedrine pills were given they were generally aware of the fact due to the subjective feeling produced.

GROUP II

No Pills	Trials 1 to 4	14.7, 18.0, 17.3, 18.0
Benzedrine Sulphate	Trials 5 to 7	21.7, 21.3, 21.3
Lactose Control Pills	Trials 8 to 10	22.0, 22.0, 21.0
No Pills	Trials 11 to 13	21.3, 21.0, 21.0

GROUP III

No Pills	Trials 1 to 6	26.8, 32.0, 31.2, 32.0, 32.0, 34.0
Benzedrine Sulphate	Trials 7 to 9	34.5, 36.5, 35.5
Lactose Control Pills	Trials 10 to 12	36.8, 36.0, 36.8
No Pills	Trials 13 to 15	37.0, 37.2, 36.8

By reference to the above data it will be noted that there is a general increase in the number of problems completed, due to practice, but that there is no definite trend for an increase or decrease during the trials when the benzedrine was administered. For Group I it may be noted that there was a fairly rapid increase up to trial six and then a general leveling off for the remainder of the trials. For the second group of undergraduates, Group II, a similar trend is noted: there was a fairly rapid increase to trial five and then a general leveling off. In comparing these two groups it will be noted that although the number of problems completed by the first group is nearly twice that of the other group, the trend of the evidence is surprisingly similar. In the third group of subjects, Group III, there was a gradual increase from the beginning to the end of the series without any marked irregularity for the trials in which benzedrine was administered. Thus the results from this group tends to support the evidence gathered from the two previous groups.

In order to determine whether the number of errors made by the subjects bore any relation to the conditions of testing, the average number of errors on each trial was computed for the three groups of subjects. However, the averages were found to be very irregular and seemed to bear no relation to the conditions of testing.

In an attempt to discover the effect that benzedrine had on the distribution of work, the twelve minute testing period was broken up into three units, the first four minutes, the fifth to the eighth minute inclusive, and the last four minutes. The number of problems completed by each subject at the end of each of these units was tabulated and it was found that most of the subjects did less work in the last four minutes than in either of the other four minute periods regard-

less of the conditions of testing. However, by calculating the percent decrease from the first four minutes to the last four minutes for the three groups of subjects the following results were obtained. For Group I, a 11.3 per cent decrease in the number of problems solved when benzedrine was administered, 14.0 per cent decrease for the trials when lactose was administered and 15.7 per cent decrease when no pills were administered. For Group II the decreases were 10.4 per cent with benzedrine, 20.6 per cent with lactose, and 17.6 per cent without pills. For Group III there was a decrease of 4.1 per cent with benzedrine, 0.8 per cent with lactose, and 0.2 per cent without pills. From these figures it may be seen that for the first two groups of subjects the percentage decrease is least when benzedrine sulphate was administered but for the last group of subjects the percentage decrease on the days when benzedrine was taken was greater than under either of the other two conditions of testing. From the evidence gathered in this experiment it is therefore difficult to determine whether benzedrine sulphate is an aid in maintaining a given level of work over an extended period of time. It would be interesting to study this factor further by using a longer period of testing, perhaps of twenty or thirty minutes in length.

In contrast to the objective evidence reported above, it is of interest to note the verbal reports given by the various subjects. These statements were obtained immediately previous to the period of testing and they may be used as an indication of the stimulating effect of benzedrine sulphate. The data were obtained for the ten subjects during six days of testing, three days with benzedrine and three days with lactose, thus, a total of sixty statements as to whether or not the subjects were tired and sixty statements as to whether or not the subjects were sleepy were obtained. All the subjects reported on the days when benzedrine was taken that they were not sleepy; however, on the days when lactose was taken, on only 14 of the 30 occasions did the subjects indicate that they were not sleepy. On the days when benzedrine was administered only one subject reported for a single trial that he was slightly tired, the other nine subjects consistently reported that they were not tired. On the other hand when lactose was taken the subjects reported on five occasions that they were definitely tired, and for ten trials that they were slightly tired. Additional information from the six undergraduates only was obtained as to whether they were nervous or not immediately previous to the period of testing. None of these subjects reported that they were nervous on the days when lactose was administered but on the ma-

jority of the days when benzedrine was administered the subjects reported that they were slightly nervous.

Information obtained from the subjects at the time of testing concerning the stimulating effect of benzedrine sulphate indicated that the weight of the subject may have a definite bearing on the stimulating effect of the drug. From the subjective reports an indication was also obtained that the effects of the benzedrine are less after successive dosages even though at least a one-day interval occurred between each trial for all the subjects. In general the subjects reported greater stimulation on the first day that the benzedrine was given than on any of the succeeding days when the drug was given. One other fact obtained from the subjective reports is that the greatest stimulation from the drug seemed to occur approximately one hour after the drug had been taken. It has been mentioned earlier in the report that the undergraduates were tested approximately two hours after the pills were taken and the graduate subjects were tested approximately four hours after the pills were taken. Possibly the results would be different if the testing were done sooner after the drug was taken. There was, however, definite evidence that our subjects were still overestimated at the time of testing.

From the evidence presented above the following conclusions may be made. On the average the number of problems completed in a twelve-minute testing period is not materially increased or decreased by the administration of benzedrine sulphate, and the number of errors is unaffected. In general there is a decrease from the beginning to the end of the twelve minute testing period in the number of problems completed and this diminution is not consistently affected by the administration of benzedrine. There is a subjective feeling of increased stimulation from a dosage of 20 mg. of benzedrine sulphate, and the increased stimulation is experienced for several hours with the greatest effect occurring approximately one hour after taking the drug. The benzedrine produces a subjective feeling of not being tired, but seems to produce a nervous condition in the subject, the effect being partially dependent upon the weight of the subject when equal dosages are administered. Finally, the objective evidence obtained in this study does not indicate either an increase or decrease in mental efficiency even though there is a subjective feeling of stimulation. The fact that no decrease in efficiency occurs from use of the drug may have an important bearing upon prescription of benzedrine to maintain wakefulness during prolonged mental effort. In presenting these results the authors are aware that the number of subjects studied in

this investigation was rather limited and that the greatest number of trials for any subject was only fifteen, so that the administration of the benzedrine was made before practice effects were completely reduced. However, the consistency of the results seems to indicate that these limitations were not serious.

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